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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/576,944	05/22/2000	Terry B. Strom	1440.1024-001	2729

21005 7590 10/14/2003

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	15

DATE MAILED: 10/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/576,944	Applicant(s) Strom
	Examiner Gamber	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 11/17/02 & 8/8/03

2a)☐ This action is **FINAL**. 2b)☑ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 1-11, 14-24, 24-28

4a) Of the above claim(s) _____ is/are withdrawn from consideration. 12-13, 15-21

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 11, 14, 22, 24-28

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☑ objected to by the Examiner. SEE OFFICE ACTION

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☑ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☑ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

PAPER NO. 15

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.
Applicant's submission filed on 8/8/03 (Paper No. 14) has been entered.

Applicant's amendment, filed 12/27/02 (Paper No. 11), has been entered.
Claims 12, 13 and 23 have been canceled.
Claims 11, 14, 22, 24, 26 and 27 have been amended.
Claim 28 has been added.

Claims 11, 14, 22, 24-28 are being acted upon as the elected invention.

Applicant is invited to clarify the status of claim 25.
It does not appear that applicant has canceled claim 25 in Paper No. 11, filed 12/27/02.
However, applicant's Paper No. 11, filed 12/27/02, does not address the status of claim 25.

Again, applicant's previous election of Group II (claims 11-14) and the species B (anti-CD40L antibodies) in Paper No. 5 has been acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

This restriction requirement is hereby reiterated. Accordingly, claims 1-10 and 15-21 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a nonelected invention and species.

With respect to applicant's previous traversal on the species of anti-CD40 antibodies, anti-CD40L antibodies, CD40-Ig and CD40L-Ig that no serious burden is placed on the examiner; MPEP 803 states that the Inventions be either independent or distinct and a burden on the Examiner if restriction is required. For the reasons of record, the structures of these costimulation blockade agents are distinct.

2. This Office Action will be in response to applicant's arguments, filed 12/27/02 (Paper No. 11).
The rejections of record can be found in the previous Office Actions (Paper Nos. 5/9/12).

3. Formal drawings, filed 5/18/98, comply with 37 CFR 1.84.
Please see the form PTO-948 previously sent in Paper No. 6.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Applicant's comments that a formal figure will be submitted upon allowance of the claims in Paper No. 11, filed 12/27/02.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in ABANDONMENT of the application.

4. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Upon reconsideration of applicant's amended claims, filed 3/29/02 (Paper No. 8), the previous rejection under 35 U.S.C. 112, first paragraph, scope of enablement, has been withdrawn.

6. Claims 11, 14, 22, 24-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

The claims encompass "biologically active derivatives of rapamycin", "fungal derivatives" and "bacterial. derivatives" and "antibodies to lymphocytes"

Page 14, paragraph 3 of the instant specification discloses that "derivatives" encompass modified agents which include alterations in amino acid sequences as well as truncated and hybrid forms of agents.

However, there is insufficient guidance and direction as to the correlation between the chemical structure and the desired binding and inhibitory function of the claimed genus of "fungal derivatives" and "bacterial derivatives" and "antibodies to lymphocytes" as well as the claimed "biologically active derivatives of rapamycin".

There is insufficient guidance and direction as to what is the nature of the structural and functional constraints on the claimed "derivatives" or the specificity of the claimed "antibodies" and, in turn, what is the predictability of making and using such "derivatives" or "antibodies" in a manner consistent with the disclosed utilities. The skilled artisan would not predict that any fungal derivative or bacterial derivative, rapamycin derivative or antibody to lymphocyte would be useful as immunosuppressives at the time the invention was made.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of "derivatives" broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein / peptide's amino acid sequence and still retain similar biological or pharmaceutical activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, the problem of predicting protein structure from the mere disclosure of generic terms of "fungal derivatives" and "bacterial derivatives" and "antibodies to lymphocytes" as well as the claimed "biologically active derivatives of rapamycin" and, in turn, utilizing predicted structural determinations to ascertain functional aspects of these fungal derivatives" and "bacterial derivatives" and "antibodies to lymphocytes and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications of other types and positions within the protein's sequence where amino acid modifications can be made with a reasonable expectations of success in obtaining similar biological or pharmaceutical activity are limited in any protein and the result of such modifications is unpredictable based on the instant disclosure. One skilled in the art would expect any tolerance to modification shown for a given protein or peptide to diminish with each further and additional modification, e.g. multiple substitutions. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acids modification in such proteins.

Minor structural differences among structurally related compounds or compositions can result in substantially different biological or pharmacological activities. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth

Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use of the claimed "fungal derivatives" and "bacterial derivatives" and "antibodies to lymphocytes" as well as the claimed "biologically active derivatives of rapamycin" in manner reasonably correlated with the scope of the claims broadly including any number of modifications of a broad range of "fungal derivatives" and "bacterial derivatives" and "antibodies to lymphocytes" as well as the claimed "biologically active derivatives of rapamycin". The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made in the "derivative" or "antibody" structure or specificity and still maintain biological and pharmaceutical activity as an immunosuppressive is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and Ex parte Forman, 230 USPQ 546 (BPAI 1986).

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective adhesion-based and/or antibody-based therapies, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for inhibiting diseases commensurate in scope with the claimed methods with inhibitory CD40-specific antibodies.

Applicant's comments on the previous rejection under 35 USC 112, first paragraph, written description are acknowledged. Upon reconsideration, applicant should address the issues under how to make and to use under 35 USC 112, first paragraph, enablement with respect to the claimed "fungal derivatives" and "bacterial derivatives" and "antibodies to lymphocytes" as well as the claimed "biologically active derivatives of rapamycin", given the limited disclosure of the instant application as filed.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 11, 22, 24, 25 and 27 are rejected under 35 U.S.C. § 102(e) as being anticipated by Chen et al. (U.S. Patent No. 5,990,109) (see entire document).

Chen et al. teach compositions comprising at least CD40L-specific antibodies and immunosuppressive agents comprising rapamycin (see entire document, including Detailed Description of the Invention, particularly column 21, paragraphs 1-3 and claims 37-38). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced antibodies and immunosuppressive agents. Although, the term "kit" is not specifically taught by the reference, there is no recitation that separates the prior art compositions comprising the same active ingredients as the instant claims.

Applicant's arguments, filed 12/27/02 (Paper No. 11), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant argues that Chen et al. do not disclose compositions comprising at least CD40L-specific antibodies and immunosuppressive agents. However, applicant acknowledges that Chen et al. does disclose heterocyclo-substituted imidazopyrazine compounds and compositions employed as protein tyrosine kinase inhibitors. Applicant also acknowledge that the compounds may be employed alone or in combination with each other as suitable therapeutic agents. Applicant acknowledges that the exemplary blocking agents include CD40:CD40L inhibitors. Applicant argues that Chen et al. does not disclose or claim composition of such agents which do not also include heterocyclo-substituted imidazopyrazine compounds and do not disclose kits.

However, Chen et al. does disclose compositions comprising rapamycin (see column 21, paragraphs 1-3, including column 21, lines 37-38).

For examination purposes, the phrase "consisting essentially of" is being interpreted as being inclusive or open - ended which does not exclude additional unrecited elements, provided that the additional elements do not materially affect the basic and novel characteristic(s)" of the claimed invention. See MPEP 2111.03.

Further, it is noted that the claimed methods recite "comprising" and "consisting essentially of" leaves the claims open for the inclusion of heterocyclo-substituted imidazopyrazine compounds.

Again applicant has not distinguished the prior art teaching of compositions from the claimed recitation of "kit", wherein the prior art compositions comprising the same active ingredients as the instant claims.

. Applicant's arguments are not found persuasive

10. Upon reconsideration of applicant's arguments, the previous rejection under 35 U.S.C. § 102(e) as being anticipated by Nadler et al. (U.S. Patent No. 5,962,415) has been withdrawn.

11. Claims 11, 14, 22 and 24-28 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Noelle et al. (U.S. Patent No. 5,942,229) in view of Chen et al. (U.S. Patent No. 5,990,109), Nadler et al. (U.S. Patent No. 5,962,415), Kelly et al. (U.S. Patent No. 5,118,493) (1449) and Strom et al. (Therapeutic Immunology, Austen et al. (Ed.) Blackwell Science, Cambridge MA, 1996; see pages 451-456) essentially for the reasons of record.

Applicant's arguments, filed 12/27/02 (Paper No. 11), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal concerning the teachings of Chen et al. are essentially the same as set forth above.

Applicant's arguments concerning the teachings of Chen et al. with respect to heterocyclo-substituted imidazopyrazine compounds that these inhibitors do not share the same properties of applicant's claimed costimulation blockade agents is acknowledged. In addition, applicant argues that Chen et al. et al. focuses on agents that are not agents claimed by applicant.

However, the teachings are clear in that compositions comprising inhibitors, including immunosuppressive agents of diverse structures, biological and pharmacological activities can be combined, given the desired endpoints of inhibiting targeted responses of interests.

Similarly, Nadler et al. teach compositions comprising at least CD40L (gp39)-specific inhibitors and immunosuppressive agents comprising rapamycin (see entire document, including Detailed Description of the Invention, particularly column 8, paragraphs 1-3).

Clearly, the prior art taught that both rapamycin and CD40L-specific inhibitors, including CD40L-specific antibodies were useful as immunosuppressants, including the inhibition of graft rejection and that both rapamycin and CD40L-specific antibodies could be combined with other immunosuppressants to achieve the desired immunosuppression.

Again, Noelle et al. teach the coadministration of two immunosuppressive agents comprising CD40L-specific antibodies (see columns 10-11, Section V) as well as art known compositions (see columns 8-10, Section IV.)and immunosuppressants (see entire document).

Noelle et al. differs from the claimed invention by teaching art known immunosuppressant rapamycin per se and by not disclosing the use of fish oils as the type of oil suitable for the compositions or formulations taught for immunosuppression.

In contradistinction with Chen et al. and Nadler et al., Noelle et al. provides the expectation of success and motivation that CD40L-specific antibodies was a key ingredient of immunosuppressive formulations.

Kelly et al. teach the use of fish oils for immunosuppressive agents such as cyclosporin (see entire document).

Given the reduced nephrotoxicity associated with fish oils with immunosuppressive agents as taught by Kelly et al.; one of ordinary skill in the art at the time the invention was made would have been motivated to select such fish oils as a suitable oil for immunosuppressive compositions and formulations as taught by de Noelle et al., Chen et al. and Nadler et al. in immunosuppressive regimens.

In further evidence, the use of immunosuppressive therapy relies upon a number of basic principles as set forth in newly added Strom et al. (Therapeutic Immunology, Austen et al. (Ed.) Blackwell Science, Cambridge MA, 1996; see pages 451-456). These principles include that different agents are used, each of which is directed at a different molecular target and aimed at interrupting several discrete stages in the immune activation pathway, including the expectation of achieving additive-synergistic effects (e.g. see page 451 and Figure 36.1). A basic principle includes the appropriate reduction or withdrawal of an immunosuppressive drug when that drug's toxicity exceeds its therapeutic benefit (page 451, column 2, lines 1-4). Strom et al. concludes that more refined immunosuppressive regimens including targeted discrete steps in antigen recognition, signal transduction and effector immunity are anticipated in clinical application (see page 455, column 2, paragraph 2).

Therefore, the combined references recognized the use of combined immunosuppressive therapy, wherein the immunosuppressive reagents are structurally different and are directed against divergent targets. Further, the combined references support compositions comprising, consisting essentially and consisting of different immunosuppressive agents, including rapamycin and anti-CD40L antibody.

The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and not is it that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). See MPEP 2145.

The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. See MPEP 2144.

Applicant's asserts that the instant invention is drawn to the discovery that rapamycin does not block the IL-2 dependent activation-induced cell death required for enduring tolerance and that many experts believed that immunosuppressive agents could be administered with costimulation blockade agents to achieve permanent engraftment.

Tufveson et al. (Immunological Reviews 136: 99-109, 1993) disclose: "A main problem in the rodent model for organ allografting is the ease with which rejection is usually suppressed" (page 100, paragraph 2). Here, Tufveson et al. disclose that the mouse widely used technique to test immunosuppressants for organ transplantation has been heterotopic cardiac grafting in rodents.

It is noted that applicant's instant application relies upon a single exemplification of a mouse heart model

Applicant's asserted unexpected results are not supported by either the objective evidence of record nor the scope of the claimed invention.

Further, the combined references provide sufficient motivation and expectation of success in combining rapamycin and anti-CD40L in the treatment of certain conditions such as transplantation and GVHD at the time the invention was made.

As indicated above, Strom et al. concludes that more refined immunosuppressive regimens including targeted discrete steps in antigen recognition, signal transduction and effector immunity are anticipated in clinical application (see page 455, column 2, paragraph 2) (Therapeutic Immunology, Austen et al. (Ed.) Blackwell Science, Cambridge MA, 1996; see pages 451-456). Such immunosuppressive regiments include that different agents are used, each of which is directed at a different molecular target and aimed at interrupting several discrete stages in the immune activation pathway, including the expectation of achieving additive-synergistic effects (e.g. see page 451 and Figure 36.1). A basic principle includes the appropriate reduction or withdrawal of an immunosuppressive drug when that drug's toxicity exceeds its therapeutic benefit (page 451, column 2, lines 1-4).

While the claim recites a kit, no positive recitation of the ingredients distinguishes it over the references; therefore the kit is encompassed by the references. However, if this is not the case, it was a well known convention in the art to place these components in a kit for convenience and economy. Such kits standardize the reagents for optimization and to facilitate the necessary strict compliance with methods of treatments.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

12. Claims 14, 24 and 28 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Noelle et al. (U.S. Patent No. 5,942,229) in view of Chen et al. (U.S. Patent No. 5,990,109), Nadler et al. (U.S. Patent No. 5,962,415), Kelly et al. (U.S. Patent No. 5,118,493) (1449) and Strom et al. (Therapeutic Immunology, Austen et al. (Ed.) Blackwell Science, Cambridge MA, 1996; see pages 451-456)
as applied to claims 11, 14, 22 and 24-28
and further in evidence of Magolda et al. (U.S. Patent No. 6,110,910).

The teachings of the references differ from the claimed invention by not explicitly teaching "kits".

As pointed out above, while the claim recites a kit, no positive recitation of the ingredients distinguishes it over the references; therefore the kit is encompassed by the references. However, if this is not the case, it well a well known convention in the art to place these components in a kit for convenience and economy.

In further evidence, Magolda et al. teach the well known use of pharmaceutical kits comprising different components as well as instructions and guidelines for administration (see column 46, paragraph 3). Magolda et al. Teach the use of various immunosuppressive agents, including rapamycin and antibodies for the treatment of various immunomodulatory disorders, including organ transplantation rejection and GVHD (see column 46, paragraph 4 - column 49, paragraph 3).

Therefore, Magolda et al. Provide support for the well known convention in the art to place these components in a kit for convenience and economy. Such kits standardize the reagents for optimization and to facilitate the necessary strict compliance with methods of treatments.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9306.

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
October 14, 2003